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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/671,298	09/25/2003	Debashish Datta	LPN-113	3136
909	7590	08/18/2005	EXAMINER	
PILLSBURY WINTHROP SHAW PITTMAN, LLP P.O. BOX 10500 MCLEAN, VA 22102			BERCH, MARK L	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 08/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/671,298

Applicant(s)

DATTA ET AL.

Examiner

Mark L. Berch

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 200063214

A1.

This reference is the equivalent of 6,552,186 discussed in the specification; see step ii' in claim 1. For reasons set forth below, claim 18 is not entitled to even the instant filing date. And even if it were entitled to the 9/17/2003 date, the 10/26/2000 date of the reference would make it an anticipation.

Claim 18 is rejected under 35 U.S.C. 102(a, e) as being anticipated by 6919449.

See example 4, steps III and IV, which anticipates for R=silyl. The first step, is seen at column 8, lines 42-48, and note that the activation produces a compounds with Y'

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as Cl. Next, the desilylation is seen in the quenching at column 8, lines 49-52. The last step (cyclization) is at lines 57-65.

Even if the claim were entitled to the 9/17/2003 date, the reference would still be available under 102(e). Note that the date under 102(a) is 10/23/2003.

Other claims are not rejected over the prior art. No reference shows the procedure of taking the isolated acid, and then converting it to the amine, and then amine to Na salt to purify it.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over EP 30294 in view of USP 5109131, EP 842937, 6384215, 6458949, 6919449, 4423213, 4427674, 4452851, 4585860, or 4631274.

See example 1 of EP 30294. Page 16, lines 13-18 shows the di-silylation of the starting material. This was acylated at lines 18-24, which gives the material of Formula II. Then the desilylation was done with water (page 16, line 26) to give the product at sentence bridging pages 16-17. That product corresponds to the intermediate formed at the end of the first step of claim 18. The cyclization with thiourea is done at page 13, lines 3-8. There are two differences between this process and that of claim 18:

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- A. The prior art uses for the cyclization-with-thiourea step, ethanol (page 13, line 7), but claim 18 uses a mixture of an organic solvent and water.
- B. The product of the cyclization-with-thiourea step is recovered as the hydrobromide salt in the prior art, but claim 18 calls for recovery in the free form. Note that there is an NH_2 group on the thiazole ring, which forms a salt with HBr. These two differences are probably connected.

The secondary reference USP 5109131 teaches both features. The use of a solvent mixture of water plus an organic solvent is taught at column 10, lines 48-53. In the working example, the cyclization-with-thiourea is done at column 13, lines 28-29 using a 1:1 mixture of THF and water. The form of the product is not identified, however. Instead, it is reacted with NaCl to give the Na salt. Thus, it must have been in the free form. If it had been as the HBr salt, a base, e.g. NaOH would have been needed to give the salt. Note that the additional step of conversion to Na salt appears in the last line of claim 18.

6458949 provides a similar procedure. See Example 1, Stage II, in which the cyclization-with-thiourea is done using a mixture of THF and water. The form of the product is not identified, however, it could not have been in the acid form, given that acid was added to the solution.

6919449, example 4, step (IV) is similar. Again, given that acid was added to the solution, the material would not have been in the acid salt form.

4423213 has in examples 315 and 316 a similar procedure using a mixture of THF and water. The product is recovered in the free form. In 4452851, see examples 9 and 10; in 4585860, examples 168 and 169; in 4631274, examples 13 and 14 with similar processes using THF/water.

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In 4427674, see ex 36, step 4, which has ethanol and water, and example 38, which has THF, ethanol and water, with the product again collected in the free form.

In EP 842937, note the scheme on page 5. This shows the use of aqueous ethanol. The product (I) is shown as clearly being in the free form. In the actual example, the compound is then converted into a formic acid solvate and subsequently into a acetone solvate. Solvates are provided for in claim 18, line 3, but even without it, this secondary reference teaches that it is conventional to do the cyclization with thiourea in a mixture of ethanol and water and obtain the product in the free form.

In 6384215, note scheme 2. See Example II, method-II. This again shows the cyclization with thiourea done with a mixture of THF and water. The product was again recovered in its free form.

There are other references as well. Although the primary reference did not happen to use water with the organic solvent to get the compound in the free form, the numerous secondary references show that such a procedure is entirely conventional, and thus using it would be obvious.

Specification

The page 9 description of EP 5567678 is not believed to be accurate. The reference does not have the thiourea process. The section should be reworded or applicants should show where in the reference this material is present.

In view of the actual claims which issued from 10/119548, the interference request is clearly moot.

Applicants' attention is drawn to 2005/0027118. The processes appear to be similar. As the examiner sees it, there are these differences:

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A. The acylation is done in 10671298 “in the presence of an acid-scavenging agent” (step i¹).

No such agent is mentioned in the claims of 2005/0027118, nor is one used in the examples.

B. In 10671298, the acylating agent is subject to two specific purity limitations, one for overall purity, and one limiting the amount of di- or poly-bromo impurities present. No such limitation appears in 2005/0027118.

C. The cyclization in 2005/0027118 is done in an aqueous solution (step iv), the organic solvent (methylene chloride) having been specifically removed in step iii. In 10671298, the organic solvent (not specified) is specifically present, not being removed until after the cyclization has been done. This issue is especially important since the cyclization-with-thiourea step being done in a mixture of water plus a water-immiscible solvent here is the point of novelty over the prior art.

D. The quenching procedures are different. 2005/0027118 quenches in step ii using either just water, or water plus sodium carbonate. 10671298 quenches in step ii¹ with a mixture of water and a water-immiscible solvent.

E. The cyclization in 10671298 is done with the acid, in the presence of the alkali metal base at a pH of 5.0-5.5. In 2005/0027118, the acid is first completely converted to Na salt, and then the cyclization is done. It is not clear whether this is a meaningful difference.

F. The free acid is crystallized out at non-overlapping pH ranges. In 2005/0027118, it is done at 1.5-2.5; in 10671298, it is done at 3.6-4.0. The gap between these is larger than either range itself.

G. In 2005/0027118, the acid is converted directly into the Na salt. In 10671298, this is not done. The acid is converted into an amine salt at a very narrow pH range, and then this

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amine salt undergoes salt exchange to produce the Na salt. Thus, the 10671298 process employs an amine intermediate which is not present in 2005/0027118.

H. Probably as a result of the difference in G, the final product is obtained slightly differently. In 2005/0027118, the salt is prepared in water, and then an organic solvent is added to precipitate it. In 10671298, the exchange is done in a mixture of water and an organic solvent.

I. 10671298 has a purity limitation and a "low color" limitation on the product; no such limitations appear in the claims of 2005/0027118.

Applicants' views are sought as to whether these two processes are patentably distinct, especially with respect to the larger differences, points A, C, F and G.

Applicants' attention is drawn to 6969449, especially example 4. The processes appear to be similar. As the examiner sees it, there are these differences: Factors A, B, D (just water is used), F (the patent uses 3.0, which is outside the 3.6-4.0 range used here), G and I listed above apply here as well. In addition:

J. The acylation is done here in a narrow range of -10°C to 0°C ; the patent does it at -30°C , although the patent claims are broad enough to embrace the range here.

Applicants' views are sought as to whether these two processes are patentably distinct, especially with respect to the larger differences, points A, F and G.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it

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is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. The term, "substituents useful in cephalosporin chemistry" is indefinite. Useful at what time --- at the time of filing? At the priority date? At the time the application is allowed? At the time the patent issues? And, useful as determined by, or known by, whom?
2. Further, "useful" how? How would one of ordinary skill in the art determine that a given choice was not "useful"? How does one demonstrate the negative?
3. In the Y' definition, what does "forms a basis that" mean? It is impossible to tell just what Y' actually is. The compound should be in reactive form, but since Y = halogen, the compound is already in reactive form, so there really isn't an effective definition for Y'.
4. The intended meaning for "silyl" is unclear. Silyl is SiH_3 , the group formed by the removal of a H from Silane, SiH_4 and is a term analogous to methyl, CH_3 . It does not appear likely that such a group is intended.
5. The third from last line of claim 18 should be "optionally desilylating", since II doesn't necessarily have any silyl present.
6. The material at the bottom right on Formula II is illegible. COOR'_E is assumed.
7. The end of claim 18 gives just the acid. But Formula I provides also for salts and esters. How are these to be obtained in a process which does not specifically provide for them?

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Claims 1-17, 19-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. The "containing ..." limitation in step i¹ is unclear. Does it apply just to impurities or to (IV) as well? That is, does it bar the use of X=Y=Br? The claim language could be read either way.
2. Step iii³ is unclear. There is supposed to be an inorganic base present in a reaction done at pH =5-5.5. That is an acid range. The acid will destroy the base, or the base will raise the pH out of that range or both.
3. Formula VII in claim 1 is in error; it should be QH⁺, not Q⁺. Likewise in claim 21.
4. Both limitations in next to last line of claim 1 are unclear. What is the standard for "substantially"? For "low"? Terms of degree, such as "substantial" or "relatively" are indefinite when the specification contains no "explicit guidelines" to distinguish from things which are not so, *Ex parte Oetiker*, 23 USPQ2d 1651, 1655 (1990) and *Ex parte Oetiker*, 23 USPQ2d 1641, and *Seattle Box Co. v. Industrial Crating & Packaging, Inc.* 221 USPQ 568, 574.
5. Claim 4 is unclear because of "preferred". Does the claim embrace anything else? If not, the word should be deleted. If so, what else, and indeed, how does it limit claim 1?
6. Regarding claims 8 and 10 the word "preferably" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

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7. The listing of lower alkyl esters of acetic acid as being immiscible in water is mistaken.

The two most important, methyl and ethyl, are both fairly miscible with water. As evidence there is cited US 20050065316 A1; see paragraph 176.

8. The term "carrier" in step vi¹ (and in claim 15 and 22) is unclear. What is a "metal carrier"? Is "base" or "salt" intended?

9. The preamble to claim 19 and Formula II indicates that it is the preparation of the sodium salt. But the last step has M, where M is any alkali metal. This inconsistency must be fixed by either changing the definition of M or changing Formula II.

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This claim goes far beyond what the specification teaches. X is very broad, but the specification makes no mention of other than the ceftriaxone side chain. Similarly, R1 is broadly defined, but the specification has only methyl. The choice of R=H is not seen in the specification as a substrate for the acylation. The specification requires COOSi(Me)₃ at the 4 position, but Claim 18 will permit ordinary esters such as the phenyl ester. There are other differences as well.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438,

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164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 18 of copending Application No. 10830806. Although the conflicting claims are not identical, they are not patentably distinct from each other because both cases cover the same process. The claim 18 in 10671298 is just a little broader than the one in 10830806.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Objections

Claim 1 must end in a period.

Claim 6 is improperly multiply dependent on claim 4, as claim 4 is itself multiply dependent.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 571-272-0663.

The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Mark L. Berch
Primary Examiner
Art Unit 1624

7/27/05